

## REMARKS

The specification has been amended to correct an editorial error discovered by Attorneys for Applicants during review of the application.

Claims 27-30, 33-40, 42-54, 59-68, 73-75, 84-85 and 90-104 were pending in the application. In the Office Action mailed March 31, 2004, claims 27-30, 33-40, 42-54, 59-68, 73-75, 84-85 and 90-104 are rejected. In the present Amendment, claims 28 and 68 have been canceled, without prejudice, and claims 27, 29-30, 37, 39, 42, 67 and 91-94 have been amended to clarify the invention. Upon entry of the above-made amendments, claims 27, 29-30, 33-40, 42-54, 59-67, 73-75, 84-85 and 90-104 will be pending in the application.

Claims 27, 67, 91 and 93 have been amended to clarify that the predetermined sequence is complementary to at least a hybridizable portion of the target polynucleotide sequence, i.e., complementary to either a portion or the entire target polynucleotide sequence. Support for the amendment is found in the specification at, e.g., page 16, lines 31-35; page 19, lines 8-21; and page 22, lines 9-11.

Claims 29, 37, 39, 42, 92 and 94 have been amended to clarify that the target polynucleotide sequence in the first sample is a sequence from a gene or gene transcript (emphasis added). Support for the amendment is found in the specification at, e.g., page 14, lines 34-46; and page 29, lines 19-26.

Claim 30 has been amended to clarify that the second sample comprise nucleotide sequences from a plurality of genes or gene transcripts of a cell or organism (emphasis added). Support for the amendment is found in the specification at, e.g., page 32, lines 10-16 and 17-22.

Claim 90 has been amended to delete dependency on the canceled claims 28 and 68.

No new matter has been added by these amendments. Entry of the foregoing amendments and consideration of the following remarks are respectfully requested.

### THE REJECTION UNDER 35 U.S.C. § 102 SHOULD BE WITHDRAWN

Claims 27-30, 33-36, 38, 40, 43-54, 59-60, 64-65, 67-68, 73, 90-91, 93 and 95-104 are rejected under 35 U.S.C. § 102(b) as being anticipated by Lo et al., U.S. Patent No.

4,900,659 (“Lo”). Applicant respectfully disagrees with the Examiner for the reasons presented below.

A claim is anticipated under 35 U.S.C. § 102 only if each and every element and limitation as set forth in the claim is found, either expressly described or inherently present, in a single prior art reference. *Glaxo, Inc. v. Novopharm Ltd.*, 52 F.3d 1043, 1047 (Fed. Cir. 1995). There must be *no differences* between the claimed invention and the reference disclosure as viewed by a person of ordinary skill in the field of the invention. *Scripps Clinic & Research Fdn. v. Genentech, Inc.* 927 F. 2d. 1565, 1576 (Fed. Cir. 1991).

The present invention relates to methods of evaluating a binding property of a polynucleotide probe comprising a predetermined nucleotide sequence complementary to at least a hybridizable portion of a target nucleotide sequence. The methods involve determining a ratio of the amount of hybridization of polynucleotides in a first sample to the polynucleotide probe and the amount of hybridization of polynucleotides in a second sample to the polynucleotide probe, and using the ratio as a measure of the binding property. The first sample comprises a plurality of polynucleotide molecules comprising the target nucleotide sequence. In some embodiments, e.g., embodiments as claimed in claims 27 and 67, at least 75% of the polynucleotide molecules in the first sample are polynucleotide molecules comprising the target nucleotide sequence. The second sample comprises a plurality of different polynucleotide molecules, each of which comprises a sequence that is different from the nucleotide sequences of any other polynucleotide molecules in the plurality of different polynucleotide molecules. In some embodiments, e.g., the embodiment as claimed in claim 91, the second sample comprises a plurality of different polynucleotide molecules each of which comprises a sequence that is different from the nucleotide sequence of any other polynucleotide molecule in the plurality of different polynucleotide molecules while does not comprise the target nucleotide sequence. Thus, the present invention relates to methods of evaluating a binding property of a probe having a specific, known sequence, i.e., a predetermined nucleotide sequence complementary to at least a hybridizable portion of a target nucleotide sequence, which make use of the hybridization levels of samples designed based on the specific probe sequence, i.e., a first sample comprising polynucleotide molecules comprising the target nucleotide sequence of the probe, and a second sample comprising polynucleotide molecules having different sequences.

Lo teaches nucleotide sequences that are specific for *N. gonorrhoeae* as versus *N. meningitidis*. For example, Lo teaches that the ratio of the amount of its nucleotide sequences hybridized to chromosomal DNA of *N. gonorrhoeae* to the amount of the nucleotide sequences hybridized to chromosomal DNA of *N. meningitidis* may be greater than 5, 25, or 50. Lo does not teach what are the base sequences of these nucleotide sequences. However, Lo teaches methods for obtaining such nucleotide sequences. In Lo, *N. gonorrhoeae* chromosomal DNA is digested into fragments (see, Lo, col. 5, Section A). Each of the fragments is inserted into a vector to form a recombinant molecule (see, Lo, col. 6, Section B). The recombinant molecule is transformed into a suitable host, e.g., *E. coli* (Lo, col. 6, Sections C and D). The recombinant molecules are amplified (Lo, col. 7, Section E). The recombinant molecules are then screened against *N. gonorrhoeae* and *N. meningitidis* chromosomal DNAs to identified those sequences that are specific for *N. gonorrhoeae* (Lo, col. 8, Section F). The screening is carried out using test dots each consisting of denatured purified chromosomal DNA from either *N. gonorrhoeae* or *N. meningitidis*, i.e., each test dot consists of chromosomal DNA from one strain of *N. gonorrhoeae* or *N. meningitidis* (Lo, col. 8, lines 13-19). Each test dot comprises fragments of chromosomal DNA that is isolated from cells and sheared (Lo, col. 8, lines 32-36). A recombinant molecule is identified if the ratio of its hybridization amount to a test dot containing fragments of chromosomal DNA of a strain of *N. gonorrhoeae* and its hybridization amount to a test dot containing fragments of chromosomal DNA of a strain of *N. meningitidis* is greater than a preset value, e.g., 5 (Lo, col. 10, lines 55-67).

In the Office Action mailed March 31, 2004, the Examiner contends that Lo's recombinant molecules can be viewed as the polynucleotide probes, and that Lo's test dots can be viewed as samples. The Examiner contends that a test dot consisting of chromosomal DNA from *N. gonorrhoeae* corresponds to the first sample of the presently claimed invention, whereas the chromosomal DNA from a plurality of strains of *N. gonorrhoeae* and/or *N. meningitidis* constitutes the second sample of the presently claimed invention (see, e.g., paragraphs 1 and 2 on page 3 of the Office Action mailed March 31, 2004). The Examiner also contends that Lo's method of screening, which involves hybridizing its recombinant molecules with test dots consisting of chromosomal DNA of a strain of *N. gonorrhoeae* and chromosomal DNA of a strain of *N. meningitidis*, respectively, and determining the ratio of the hybridized amounts, anticipates the presently claimed invention.

At the outset, Applicant respectfully submits that Lo does not teach polynucleotide probes comprising a predetermined nucleotide sequence complementary to at least a hybridizable portion of a target nucleotide sequence. It is commonly understood in the art that a predetermined sequence refers to a sequence whose nucleotide sequence has been determined. In Lo, the probes, i.e., the recombinant molecules, that specifically hybridize to *N. gonorrhoeae* are produced by fragmenting chromosomal DNA of *N. gonorrhoeae* (e.g., by restriction digestion). Each fragment of *N. gonorrhoeae* chromosomal DNA was inserted into a recombinant molecule and was screened against the test dots. Lo does not teach determining the nucleotide sequences of any of its fragments prior to the screening step. Thus, Lo does not teach that any of the fragments subjected to screening have a predetermined sequence. In the instant Office Action, the Examiner contends that “[t]he spots are each contacted with predetermined nucleotide sequence probes wherein the probes are predetermined as being fragmented chromosomal DNA from *N. gonorrhoeae* ...” (see, paragraph 2 on page 3 of the instant Office Action). If the Examiner means that Lo’s probes have predetermined nucleotide sequences because there is knowledge about the source or means of preparation of the fragments, this is an unreasonable construction because this construction is inconsistent with both the instant specification and the common meaning of the term. If the Examiner means that Lo’s probes have predetermined sequences because the nucleotide sequences are inherent in the fragments obtained, Applicant respectfully submits that such a contention is in error. Applicant respectfully points out that this would amount to an assertion that any and all DNA sequences in fragments obtained from the genome of an organism are predetermined sequences. Such an assertion is inconsistent with the common usage of the term and the instant specification.

Applicant respectfully submits that Lo’s method is designed to identify, among different probes having unknown sequences, those that exhibit specificity to *N. gonorrhoeae* as against *N. meningitidis*, not to evaluate a binding property of a probe having a specific, known sequence. Applicant respectfully submits that this distinction is not a trivial one. In Lo, it does not matter which sequence portion or sequence portions in its probe binds to one or more sequences in *N. gonorrhoeae* chromosomal DNA. For example, in Lo it does not matter whether there may be two or more different subsequences in its probe each exhibiting a different level of binding to a different target sequence, Lo only determines the overall binding, i.e., the binding of the recombinant molecule to all different target sequences. Thus, a recombinant molecule of Lo may comprise two or more different subsequences, each being

complementary to a different target sequence in *N. gonorrhoeae* chromosomal DNA. Such a recombinant molecule may have two or more different target sequences. Hybridization specificity, e.g., measured ratio, of such a recombinant molecule represents an average of hybridization specificities of these different subsequences to their respective target sequences. In fact, Lo contemplates that such is the case. For example, in Lo, col. 16, lines 16-35, Lo teaches that its recombinant molecules may comprise many different sequences, each having different specificity to *N. gonorrhoeae* chromosomal DNA. Therefore, Lo does not teach a screening method that determines a binding property of a specific sequence in a probe to a target sequence, but rather, an “average” binding property of an unknown number of unknown nucleotide sequences to their respective different target sequences. Thus, Lo does not teach a “method for evaluating a binding property of a polynucleotide probe comprising a predetermined nucleotide sequence complementary to at least a hybridizable portion of a target nucleotide sequence” as claimed in the present invention.

Further, Applicant respectfully submits that Lo’s test dot consisting of DNA fragments from *N. gonorrhoeae* does not satisfy the limitation of the first sample of the presently claimed invention. In the present invention, the first sample “comprises a plurality of polynucleotide molecules comprising said target nucleotide sequence” (see, e.g., claim 27, emphasis added). Thus, an entire target sequence must be present in at least some of the polynucleotide molecules in the first sample. In Lo, each probe, i.e., each recombinant molecule, carries a fragment of chromosomal DNA of *N. gonorrhoeae* obtained by, e.g., restriction digestion. A target sequence for such a probe would be a nucleotide sequence that is complementary to a particular sequence in the *N. gonorrhoeae* fragment in the recombinant molecule. On the other hand, in Lo, each test dot also consists of fragments of chromosomal DNA from a strain of *N. gonorrhoeae*. Such fragments are produced by shearing (see, Lo, col. 22, lines 16). Thus, each polynucleotide molecule in Lo’s first sample, i.e., the *N. gonorrhoeae* test dot, comprises a DNA fragment produced by shearing. Lo does not teach that any of these polynucleotide molecules, i.e., DNA fragments, comprise a particular sequence. That is, Lo does not teach that the sequence of any of the fragments encompasses a particular sequence in its entirety. Nor is this limitation inherent in Lo. It is well-known that shearing produces random fragments. Thus, in the test dot of Lo, there is no certainty that any fragment necessarily comprises any particular target sequence in its entirety, and, since such is not inevitable in Lo, the test for inherency has not been satisfied. For example, the court held in *Continental Can Co. v. Monsanto Co.* that

Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient. [Citations omitted.]

*Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264 (Fed. Cir. 1991), quoting *In re Oelrich*, 666 F.2d 578 (CCPA 1981). Here, because shearing results in random fragments, Lo's probes do not inherently comprise particular sequences. Thus, Lo's *N. gonorrhoeae* test dots are not the "first sample" of the claims.

Additionally with respect to claims 27 and 67, Lo does not teach, expressly or inherently, that Lo's *N. gonorrhoeae* test dot contains at least 75% polynucleotide molecules that comprise a target sequence to which a predetermined nucleotide sequence of the fragment is hybridizable. In the randomly generated sheared fragments of Lo, the sample would not necessarily contain at least 75% polynucleotide molecules that comprise a particular target sequence. Applicant also notes that each of Lo's different recombinant molecules is a different probe. Using the Examiner's rationale, since Lo uses the same *N. gonorrhoeae* test dot (i.e., first sample) for screening all its probes, at least 75% of the fragments in its *N. gonorrhoeae* test dot would have to comprise each target sequence. It is unreasonable to expect this to be the case.

Applicant also respectfully submits that Lo does not teach a second sample which comprises chromosomal DNA from a plurality of different strains of either *N. gonorrhoeae* or *N. meningitidis*. As discussed above, Lo teaches that each individual test dot, i.e., each sample, consists of fragments from one strain of either *N. gonorrhoeae* or *N. meningitidis*. Lo does not teach a test dot that comprises a mixture of chromosomal DNA from two or more different strains. In Lo, hybridization to individual dots is used in the screening of the recombinant molecules. Thus, Lo does not teach a second sample comprising "chromosomal DNA from *N. gonorrhoeae*, strains 53415, 53416, 53417, 53418 and 53419 and chromosomal DNA from *N. gonorrhoeae*, 53420, 53421, 53422, 53423, 53424, 53425."

In summary, Lo does not teach evaluating a binding property of polynucleotide probes of specific sequences, i.e., polynucleotide probes comprising a predetermined nucleotide sequence complementary to at least a hybridizable portion of a target nucleotide sequence. Lo does not teach the use of a first sample that "comprises a plurality of polynucleotide molecules comprising said target nucleotide sequence" for evaluating the binding property of such probes. Thus, Lo does not anticipate independent claims 27, 67, 91,

and 93. In addition, with respect to claims 27 and 67, Lo does not teach a first sample in which at least 75% of the polynucleotide molecules are polynucleotide molecules comprising the target nucleotide sequence. Because Lo does not anticipate the independent claims, Lo cannot anticipate any of the dependent claims. Thus, Applicant respectfully submits that Lo does not anticipate claims 27, 29-30, 33-36, 38, 40, 43-54, 59-60, 64-65, 67-67, 73, 90-91, 93 and 95-104 (claims 28 and 68 being canceled), and that the rejection of these claims under 35 U.S.C. § 102(b) based on Lo should be withdrawn.

**THE REJECTIONS UNDER 35 U.S.C. § 103(a)**  
**SHOULD BE WITHDRAWN**

Claims 37, 39, 42, 92 and 94 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lo et al., U.S. Patent No. 4,900,659 (“Lo”). Claims 61-63, 66, 74-75, and 84-85 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lo in view of Lockhart et al., U.S. Patent No. 6,344,316 (“Lockhart”). Applicant respectfully disagrees with the Examiner for the reasons presented below.

A finding of obviousness under 35 U.S.C. § 103(a) requires a determination that the differences between the claimed subject matter and the prior art are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere*, 383, U.S. 1 (1966). The relevant inquiry is whether the prior art suggests the invention and whether the prior art provides one of ordinary skill in the art with a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be found in the prior art. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). When a rejection depends on a combination of prior art references, there must be some teaching, suggestion, or motivation to combine the references. *In re Rouffet*, 149 F.3d 1350 (Fed. Cir. 1998).

With respect to claims 37, 39, 42, 92 and 94, the Examiner contends that Lo teaches a method for screening closely related samples to analyze probes in which the method provides for screening nucleotide sequences that are specific for a “genetically distinct group.” The Examiner contends that Lo “suggests [*sic*] their method is useful for wild-type and mutants (e.g. deletion mutants). Hence, it would have been obvious to one of ordinary skill in the art ... to apply the method of Lo et al to screen genetically distinct groups (e.g. mutants and / or wild-type samples) to thereby screen and analyze mutants and/or wild-type-specific probes ...” (see, last paragraph on page 9 through page 10 of the instant Office Action).

Applicant respectfully submits that Lo does not render obvious the independent claims 27, 67, 91, and 93 of the present invention, upon which the rejected claims depend. As discussed above, Lo does not teach or suggest polynucleotide probes comprising a predetermined nucleotide sequence complementary to at least a hybridizable portion of a target nucleotide sequence. It is commonly understood in the art that a predetermined sequence refers to a sequence whose nucleotide sequence has been determined. In Lo, the probes, i.e., the recombinant molecules, that specifically hybridize to *N. gonorrhoeae* are produced by fragmenting chromosomal DNA of *N. gonorrhoeae* (e.g., by restriction digestion). Each fragment of *N. gonorrhoeae* chromosomal DNA was inserted into a recombinant molecule and was screened against the test dots. Lo does not teach determining the nucleotide sequences of any of its fragments prior to the screening step. Thus, Lo does not teach or suggest screening probes that have a predetermined sequence.

Additionally, a recombinant molecule of Lo may comprise two or more different subsequences, each being complementary to a different target sequence in *N. gonorrhoeae* chromosomal DNA. Hybridization specificity, e.g., measured ratio, of such a recombinant molecule represents an average of hybridization specificities of these different subsequences to their respective target sequences. Lo does not teach or suggest which sequence portion, or portions, in a recombinant molecule whose binding property is to be evaluated. Although Lo teaches determination of a ratio of hybridization amounts of its recombinant molecule to *N. gonorrhoeae* and *N. meningitidis*, Lo does not teach or suggest that the ratio reflects the binding property of a specific probe sequence. Instead, Lo suggests that there may be many subsequences in its recombinant molecule, and that the ratio represents the overall hybridization specificity. Thus, Lo does not teach or suggest evaluating a binding property of a particular probe sequence.

Furthermore, Lo's test dot consisting of DNA fragments from *N. gonorrhoeae* does not satisfy the limitation of the first sample of the presently claimed invention. As discussed above, in the present invention, the first sample "comprises a plurality of polynucleotide molecules comprising said target nucleotide sequence." Thus, an entire target sequence must be present in at least some of the polynucleotide molecules in the first sample. In Lo, each probe, i.e., each recombinant molecule, carries a fragment of chromosomal DNA of *N. gonorrhoeae* obtained by, e.g., restriction digestion. A target sequence for such a probe would be a nucleotide sequence that is complementary to a particular sequence in the *N.*



*gonorrhoeae* fragment in the recombinant molecule. On the other hand, in Lo, each test dot consists of fragments of chromosomal DNA from a strain of *N. gonorrhoeae* produced by shearing. Lo does not teach or suggest that any of these polynucleotide molecules, i.e., DNA fragments, comprise a particular sequence in its entirety. Thus, Lo does not teach or suggest the use of a sample comprising polynucleotide molecules comprising a particular target sequence in its entirety.

Thus, Lo does not teach or suggest a method of evaluating a binding property of a polynucleotide probe of a specific sequence, i.e., a polynucleotide probe comprising a predetermined nucleotide sequence complementary to at least a hybridizable portion of a target nucleotide sequence. As discussed above, Lo does not teach or suggest such a method making use of a first sample that “comprises a plurality of polynucleotide molecules comprising said target nucleotide sequence” for evaluating the binding property of such probes. Thus, Lo does not teach or suggest the methods of the present invention as claimed in the independent claims 27, 67, 91, and 93. One of ordinary skilled person in the art would not be motivated by Lo to a method of evaluating the binding property of a probe having specific sequence using pair of samples designed based on the specific sequence. Nor would the ordinary skilled person have any expectation of success of such a method based on the teaching of Lo, as there is no suggestion or teaching of use of a first sample that “comprises a plurality of polynucleotide molecules comprising said target nucleotide sequence” for evaluating the binding property of such probes. Since Lo does not render claims 27, 67, 91, and 93 obvious, Lo cannot render claims 37, 39, 42, 92 and 94 obvious.

Furthermore, Applicant respectfully disagrees with the Examiner’s contention that because Lo teaches a method for screening nucleotide sequences using closely related species, then Lo also suggests a method of screening using a wild-type and a deletion mutant.

With respect to claims 61-63, 66, 74-75, 84-85, the Examiner contends that although Lo does not teach that the probes are fixed on an array in which different probes are attached to different locations and does not teach differentially labeling polynucleotides with fluorescent labels, Lockhart teaches fixing probes on an array and differentially labeling polynucleotides with fluorescent labels thereby providing teachings that are missing in Lo.

Lo has been discussed above. Lockhart teaches methods for identifying differences in nucleic acid abundances (e.g., expression levels) between two or more samples using high

density DNA microarrays. In Lockhart, a method of optimizing a set of probes for detection of a particular gene is disclosed. The probe optimization method involves first hybridizing the probes with their target nucleic acids alone and then hybridizing the probes with a high complexity, high concentration nucleic acid sample that does not contain the targets complementary to the probes (Lockhart, column 36, lines 30-36), and selecting those probes that show a strong hybridization signal with their target and little or no cross-hybridization with the high complexity sample as preferred probes for use in the high density arrays (Lockhart, column 36, lines 44-47). For selection of probes showing a strong hybridization signal with their target, Lockhart teaches that the probes are hybridized to a sample containing target nucleic acids having subsequences complementary to the oligonucleotide probes, and those probes are selected for which the difference in hybridization intensity between the probes and their respective mismatch controls exceeds a threshold hybridization intensity (see, e.g., Lockhart col. 37, lines 1-12). For selection of probes showing little or no cross-hybridization, Lockhart teaches that the probes can be hybridized with a nucleic acid sample that is not expected to contain sequences complementary to the probes, and those probes are selected for which both the probes and their mismatch controls show hybridization intensities below a threshold value (see, e.g., Lockhart col. 37, lines 13-27). Thus, in Lockhart, selection of probes that show a strong hybridization signal with their target and little or no cross-hybridization is achieved by evaluating a probe according to its amount of hybridization to the target sample, and comparing this amount to a threshold, and separately, evaluating the probe according to its amount of hybridization to the non-target sample, and comparing this latter amount to a second threshold value. Lockhart does not teach or suggest comparing directly the hybridization signal and cross-hybridization signal of the same probe, much less combining the hybridization signal and cross-hybridization signal of the same probe into a single quantity, e.g., a ratio, and using such a single quantity as a measure of the binding property of the probe.

As discussed above, Lo does not teach or suggest evaluating polynucleotide probes of specific sequences, i.e., polynucleotide probes comprising a predetermined nucleotide sequence complementary to at least a hybridizable portion of a target nucleotide sequence. Lo does not teach or suggest the use of a first sample that “comprises a plurality of polynucleotide molecules comprising said target nucleotide sequence; ... wherein at least 75% of the polynucleotide molecules in said first sample are polynucleotide molecules comprising said target nucleotide sequence” for evaluating the binding property of such

probes. In order for Lockhart to supplement what is missing in Lo, Lockhart would have to teach or suggest determination of a subsequence in a recombinant molecule of Lo (which binds a “target sequence” in *N. gonorrhoeae* chromosomal DNA), and determination of the respective binding properties, i.e., binding ratios, of these subsequences. Lockhart would also have to teach or suggest preparation of samples comprising chromosomal DNA fragments such that the samples satisfy the requirement of the first sample of the present invention as claimed in claims 27 and 67. Since Lockhart teaches none of these, Lockhart does not supply what is missing in Lo.

Applicant also respectfully submits that Lo and Lockhart cannot be properly combined in the manner suggested by the Examiner. Lo teaches that its samples, i.e., test dots, are fixed on a surface. Such a sample cannot hybridize with surface-fixed probes. If Lo is combined with Lockhart as suggested by the Examiner to fix the probes, i.e., the recombinant molecules, on an array, hybridization between the probes and the samples cannot be achieved. Thus, Lo in view of Lockhart does not render claims 27 and 67 obvious. As such, regardless whether Lockhart teaches fixing probes on an array or the use of fluorescent labels, Lo in view of Lockhart cannot render the dependent claims 61-63, 66, 74-75, and 84-85 obvious.

Therefore, Applicant respectfully requests that the rejection of claims 37, 39, 42, 92 and 94 under 35 U.S.C. § 103(a) based on Lo and the rejection of claims 61-63, 66, 74-75, and 84-85 under 35 U.S.C. § 103(a) based on Lo in view of Lockhart be withdrawn.

### CONCLUSION

Applicant respectfully requests entry of the foregoing amendments and remarks into the file of the above-identified application. Applicant believes that all the pending claims are

in condition for allowance. Withdrawal of the Examiner's rejections and allowance of the application are respectfully requested.

Respectfully submitted,

Date: September 30, 2004

Adriane M. Antler 32,605  
Adriane M. Antler (Reg. No.)  
**JONES DAY**  
222 East 41st Street  
New York, New York 10017-6702  
Phone: (212) 326-3939